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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/023,033 | 12/19/2001 | John J. Harrington | 1522.0010004/MAC | 5770 |

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| EXAMINER | |
|---|---|
| MARVICH, MARIA | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | |

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/023,033 | HARRINGTON ET AL. | |
| | Examiner | Art Unit | |
| | Maria B Marvich, PhD | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *67-86* is/are pending in the application.

4a) Of the above claim(s) *67-72,78 and 85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *73-77,79-84 and 86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 December 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/6/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

This office action is in response to a response to a restriction requirement filed 7/1/04. Claims 1-66 have been cancelled. Claims 67-86 are pending in the application.

### *Election/Restrictions*

Applicant's election with traverse of Group II (claims 73-77, 79-84 and 86) in the reply filed on 7/1/04 is acknowledged. The traversal is on the ground(s) that the genomic DNA that is in the chromosome of the instant invention is exogenous and is derived from a DNA fragment, the genomic DNA present in pared down chromosomes is endogenous.

Applicants' arguments in the amendment filed 11/3/03 have been considered but are not persuasive. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). During prosecution, claims must be interpreted as broadly as their terms reasonably allow. Applicants would like to rely on descriptions of the invention that are not reasonably applied to the claims as written.

The requirement is still deemed proper and is therefore made FINAL. Claims 67-72, 78 and 85 have been withdrawn from consideration as not directed to the elected invention.

### *Information Disclosure Statement*

An IDS filed 5/6/02 has been identified and the documents considered. The signed and initialed PTO Form 1449 has been mailed with this action.

***Drawings***

Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

***Priority***

In the reference to the prior application inserted, as the first sentence of the specification of this application, the current status of all nonprovisional parent applications referenced should be updated. Specifically, application 08/643,556 filed 5/6/96, is now U.S. 6,348,353.

Furthermore, support for the artificial chromosome obtained by introduction of centromeric, telomeric and genomic DNA was not found in the priority document 08/487,989. Support has been found in the priority document application 08/643,554.

Therefore, the priority date for this invention is given as the filing date, 5/6/96, of application 08/643,554.

***Double Patenting***

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 73-75, 79-82 and 86 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. 6,348,353. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claim is either anticipated by, or would have been obvious over, the reference claims. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims recite artificial mammalian chromosomes comprising telomeric, centromeric and

genomic DNA. Although the conflicting claims are not identical, they are not patentably distinct from each other because the cited claims of the instant invention are generic to all that is recited in claims 1-2 of U.S. 6,348,353. The instant claims recite an artificial mammalian chromosome prepared by the introduction into a mammalian cell centromeric, telomeric and genomic DNA in which the centromeric and telomeric DNA provides centromere and telomere function, which is not required of 6,348,353. 6,348,353 recites that the centromeric DNA is a directional, repetitive array at least 100 kb in length of either alpha satellite DNA from mammals and avians. That is, claims 1-2 of U.S. 6,348,353 anticipate and fall entirely within the scope of the rejected claims of the instant application.

Additionally, if a patent resulting from the instant claims was issued and transferred to an assignee different from the assignee holding the U.S. 6,348,353, then two different assignees would hold a patent to the claimed invention of U.S. 6,348,353, and thus improperly there would be possible harassment by multiple assignees.

***Claim Rejections - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 73-77, 79-84 and 86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 73-77, 79, 82-84 and 86 are vague and indefinite in that the metes and bounds of "centromeric, telomeric and genomic DNA fragments" are unclear.

Centromeric and telomeric DNA are components of genomic DNA so it is unclear if the "genomic DNA fragments" are distinct from the centromeric or telomeric or not.

Claim 74 and 86 are vague and indefinite in that the metes and bounds of "different source" are unclear. It is unclear if the "different source" must be a different species or different cell type or different cell. "Different" is a relative term and it is unclear how "different" the source for the genomic DNA must be.

Claim 79 is vague and indefinite in that the metes and bounds of " a sub-genomic DAN fragment" is unknown. It is unclear how "a fragment" can be selected from "fragments" generated by restriction enzyme or mechanical shearing. The Markush groups indicate more than one fragment.

Claim 80 recites the limitation "the genomic DNA fragment" in claim 79. There is insufficient antecedent basis for this limitation in the claim.

***Claim Rejections - 35 USC § 112, first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 73-77, 79-84 and 86 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim a genus of centromeric fragments and functional equivalents of alpha satellite DNA that are components of an artificial mammalian chromosome.

Applicants claim a genus of telomeric fragments as components of an artificial mammalian chromosome.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

In the instant disclosure, applicants have developed a system for the generation of artificial mammalian chromosome. The artificial mammalian chromosome are generated by the introduction of purified DNA which then forms chromosomal structures with several advantages for biological applications. Applicants teach that the centromeric DNA supports kinetechore formation and thereby enables proper chromosome segregation which appears to result from the association of the centromeric DNA during mitosis with CENP-E, a kinesin-like protein. The disclosure states that preferred embodiments of the invention involve the use of alpha satellite DNA but can be applied to any centromeric DNA that provides this function especially highly repetitive DNA (see page 19, line 14 through page 20, line 6). Exemplified centromeric fragments are alpha satellite arrays of greater than 100 kb generated by multimerization of 92 bp alpha satellite arrays from plasmids comprising 16 alpha and 17 alpha sequences. 92 kb alpha

satellite DNA is purified by digestion with BamHI and BglII of 16 alpha or 17 alpha containing plasmids each from two different sources. The alpha sequence, either 16 alpha or 17 alpha, from the two sources are ligated to one another in a 5:1 ration to generate multimers of greater than 100kb (see page 37, line 13-27). In general, applicants claim a broad genus of centromeric fragments without regard to the qualitative or quantitative nature of the fragments except to state that the centromeric fragments must provide centromere function. Applicants do not provide a correlation between the use of alpha 16 and 17 BamHI/BglII 92 kb fragments and their centromeric function. Furthermore, applicants claim a broad genus of sequences functionally equivalent to alpha satellite DNA. Specifically, it is indicated that fragments containing a CENP-B box in *M.musculus* called a minor satellite repeat unit and in *M. caroli* a 79 bp satellite sequence possess the same activity as alpha satellite DNA. However, no other functional equivalents are envisioned to function in formation of artificial mammalian chromosome. Neither applicant nor the prior art provide a correlation between the structure of the recited sequences and ability to form artificial mammalian chromosome. Given the diversity and large size of the genus of centromeric fragments and functional equivalents, and the inability to determine which will also have the recited ability, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of one or two species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of the broadly claimed genus.

Applicants teach that the telomeric DNA functions to replicate the ends of linear DNA molecules and thus telomeric fragments are required with linear chromosomes as opposed to circular chromosomes (see page 12, line 22-26). Simple (TTAGGG)n arrays

are sufficient to provide telomere function (page 22, line 14-24). For the exemplified artificial mammalian chromosome, human telomeric DNA was generated by PCR. Figure 2 describes the use of 2kb to 10kb of telomeric DNA. Otherwise, there is no indication of size requirements of the telomeric DNA fragments to provide telomeric function. Neither applicant nor the prior art provide a correlation between the structure of the recited sequences and ability to form artificial mammalian chromosome. Given the diversity and large size of the genus of telomeric fragments, and the inability to determine which will also have the recited ability, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of the broadly claimed genus.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 73-77 are rejected under 35 U.S.C. 102(b) as being anticipated by Hadlaczky (U.S. 5,288,625; see entire document).

Hadlaczky teaches the generation of stable chromosomes, which carry human centromeric sequences, and cell lines that carry the chromosomes (see e.g. abstract). The centromeres are linked to selectable markers (see e.g. column 1, line 58-64) which is genomic DNA from a source different from the centromeric DNA. Telomeric DNA sequences (TTAGGG repeats) were found colocalized with the minichromosomes (see e.g. column 6, line 49 through column 7, line 2). Absent evidence to the contrary, the artificial chromosome of Hadlaczky comprises the same components of the artificial mammalian chromosome of the instant invention in that both have centromeric, telomeric and genomic DNA fragments in which the centromeric and telomeric fragments have centromere and telomere functions. Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claims 73-74, 76-77, 79-84 and 86 are rejected under 35 U.S.C. 102(e) as being anticipated by Hadlaczky and Szalay (US 6,743,967; see entire document).

Hadlaczky and Szalay teach the generation of artificial chromosomes that contain a megareplicon, a centromere and two telomeres. Megareplicons are tandem blocks of satellite DNA flanked by heterologous non-satellite DNA (see column 4, line 11-50).

Sites for insertion of gene coding for proteins of interest and vectors and cell lines expressing the chromosomes are provided (see e.g. column 3, line 9-20, line 34-41 and column 5, line 14-41). The satellite DNA is comprised of mouse minor satellite DNA (column 34, line 42-59) as well as alpha satellite human DNA (see e.g. column 48, line 10-14), which binds CENP. The genes of interest as well as the telomeric fragments were generated by restriction digestion (see e.g. column 47, line 8-36). The DNA comprises several replication origins (see e.g. column 40, line 27-64). Absent evidence to the contrary, the artificial chromosome of Hadlaczky and Szalay comprises the same components of the artificial mammalian chromosome of the instant invention in that both have centromeric, telomeric and genomic DNA fragments in which the centromeric and telomeric fragments have centromere and telomere functions. Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571)-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1636

July 22, 2004

GERRY LEFFERS
PRIMARY EXAMINER